THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 23

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MARTIN COLE, THOMAS T. HOWARTH
and CHRISTOPHER READING

Appeal No. 98-1591
Application 08/417,625[1]

HEARD: MAY 3, 1999

Before GARRIS, OWENS and LIEBERMAN, *Administrative Patent Judges*.

OWENS, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] Application for patent filed April 6, 1995. According to appellants, the application is a continuation of Application 07/749,482, filed August 15, 1991, which is a continuation of Application 07/210,339, filed June 23, 1988, now abandoned, which is a continuation is Application 05/569,007, filed April 17, 1975, now abandoned.

This is an appeal from the examiner's final rejection of claims 36-45, which are all of the claims remaining in the application.

THE INVENTION

Appellants' claimed invention is directed toward clavulanic acid and specified salts thereof. Appellants state that these compounds enhance the effectiveness of $-lactam antibiotics against many $-lactamase producing bacteria (specification, page 1, lines 5-7). Claim 42 is illustrative and reads as follows:

42. Clavulanic acid.

THE REFERENCE

Eli Lilly & Co. (Lilly)	1,315,177	Apr. 26, 1973

THE REJECTIONS

Claims 36, 37 and 41-45 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 35 and 36 of copending Application 08/417,628 and over claims 36-42 of copending Application
08/418,055. Claims 36-45 stand rejected under 35 U.S.C. § 103

as

being unpatentable over Lilly.[2]

OPINION

Appellants do not challenge the provisional obviousness-type double patenting rejections. We therefore summarily affirm these rejections. As for the rejection under 35 U.S.C. § 103, we have carefully considered all of the arguments advanced by appellants and the examiner and determine that claims 36, 37 and 40-45 are unpatentable. Accordingly, we affirm the rejection of these claims under 35 U.S.C. § 103. We do not, however, affirm the rejection under 35 U.S.C. § 103 of claims 38 and 39.

Regarding the rejection under 35 U.S.C. § 103, appellants indicate that claims 36, 37 and 40-45 stand or fall together, as do claims 38 and 39 (brief, page 8). Appellants state that claim 42 is exemplary of the first group of claims (brief,

[2] In the examiner's answer, the rejection under 35 U.S.C. § 103 does not include claim 45. This omission appears to be inadvertent. The final rejection (paper no. 7, page 2) included this claim in the rejection under 35 U.S.C. § 103, and appellants' discussion of the rejection under 35 U.S.C. § 103 includes claim 45 (brief, page 2). Accordingly, we consider the rejection of claim 45 under 35 U.S.C. § 103 to be before us for consideration.

page 8). We limit our consideration of the first group of claims to exemplary claim 42. *See In re Ochiai*, 71 F.3d 1565, 1566 n.2, 37 USPQ2d 1127, 1129 n.2 (Fed. Cir. 1995); 37 CFR § 1.192(c)(7)(1995).

Rejection of claims 36, 37 and 40-45 under 35 U.S.C. § 103

In the first application (Application 05/569,007) in the chain of applications which led to the present application, a claim to clavulanic acid was rejected under 35 U.S.C. § 102(b) over Lilly, and this rejection was appealed to the board. The board, in reliance upon *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977), and *In re Sussman*, 141 F.2d 267, 60 USPQ 538 (CCPA 1944), affirmed this rejection on the ground that because Lilly's fermentation broth and that of appellants are prepared in the same manner, it is reasonable to presume that Lilly's fermentation broth inherently contains clavulanic acid (exhibit 12, page 4).[3] The board stated that appellants had the burden of rebutting the presumption that Lilly's fermentation broth inherently contains clavulanic acid, and

[3] The exhibits referred to in this opinion are in the appendix to appellants' brief.

that appellants did not carry that burden (exhibit 12, page 5).

Subsequent to the board's decision, appellants submitted two declarations by Dr. Elson (exhibits 13 and 16) and one declaration by each of Dr. Hermann and Dr. Holmes (exhibits 14 and 15, respectively) which, appellants argue, show that the product produced by the Lilly process does not necessarily include clavulanic acid (brief, page 13). For the reasons set forth in the prior board decision, Lilly's process *prima facie* inherently produces clavulanic acid in the fermentation broth. In view of this *prima facie* case and appellants' rebuttal evidence thereagainst, we begin anew an analysis to determine, based on the evidence of record as a whole, whether the examiner's rejection of appellants' claim 42 over Lilly is proper. *See In re Rinehart*, 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976).

Appellants argue that in a declaration by Elson (exhibit 16), Lilly's fermentation and extraction process is reproduced as closely as possible (brief, page 18). Appellants argue that only five of fifteen separate batch

fermentations carried out following the Lilly process as closely as possible produced any clavulanic acid in the fermentation broth after 66 hours of fermentation (*see id*.). Based on this evidence, appellants argue that clavulanic acid is not inherently present in Lilly's fermentation broth (*see id*.).

One of ordinary skill in the art would have carried out Lilly's process such that the products desired by Lilly are produced as in example 17. Thus, to overcome the *prima facie* case of inherency addressed by the board in the previous appeal, appellants have the burden of showing that when the products desired by Lilly are produced using the Lilly process, clavulanic acid is not necessarily also produced. Appellants have not carried this burden.

The Elson declaration (exhibit 16) sets forth the results of four experiments, R201 to R204. In each of experiments R201 to R203, three batches were tested, whereas six batches were tested in experiment R204. The data in the declaration show that of the fifteen tests, after 66 hours of fermentation, which is the duration of the fermentation in

Lilly's example 17 (exhibit 10, page 18, line 56), six tests produced both clavulanic acid and cephamycin C which, appellants indicate, is one of Lilly's desired products (brief, page 9),[4] whereas in six tests, neither clavulanic acid nor cephamycin C was made.[5] In the remaining three tests, the data are inconclusive.[6] That is, in experiment R204 batches 50/4 and 50/8, the imidazole assay and bioassay showed no production of clavulanic acid or cephamycin C. The HPLC analysis, however, indicated that cephamycin C, but not clavulanic acid, was present. In experiment R204 batch 50/6, no clavulanic acid was detected by use of the imidazole assay, whereas clavulanic acid was detected by HPLC and cephamycin C was detected by use of both the bioassay and HPLC. It appears that the test results which indicated the presence of cephamycin C in batches 50/4 and 50/8, and the test results

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[4] Experiment R201, batches 50/6, 50/7 and 50/8; experiment R204, batches 50/3, 50/5 and 50/7. In experiment R204, batches 50/5 and 50/7, the imidazole and bioassay both showed no clavulanic acid, whereas the HPLC test indicated the presence of both clavulanic acid and cephamycin C.

[5] Experiments R202 and R203.

[6] Experiment R204, batches 50/4, 50/6 and 50/8.

which showed detection of clavulanic acid by the imidazole assay in batch 50/6, may be aberrations.

For the above reasons, the data presented in the Elson declaration (exhibit 16) are not sufficient to show that when cephamycin C is made by the Lilly process, clavulanic acid is not necessarily also produced. On the contrary, these data support the conclusion that clavulanic acid indeed is inherently produced when the Lilly process is conducted in such a manner that the products desired by Lilly are produced.

Appellants argue that Lilly's observation that the minor factors produced along with his desired A16886I and A16886II factors are similar to the A16886I and A16886II factors indicates that the minor factors are penicillin N and deacetoxycephalosporin C, because these compounds are more structurally similar than clavulanic acid to A16886I and A16886II (brief, page 14). Appellants also argue that Lilly indicates that the A16886I and A16886II factors and the minor factors can be used as an acid addition salt, whereas clavulanic acid does not form an acid addition salt (*see id*.). These arguments are not well taken because they are not directed toward the relevant issue which is not whether Lilly

thought the minor factors were clavulanic acid or penicillin N and deacetoxycephalosporin C but, rather, whether clavulanic acid is inherently produced in Lilly's fermentation broth when Lilly's desired products are produced.

Appellants argue, in reliance upon an Elson declaration (exhibit 13), that any clavulanic acid formed in Lilly's fermentation broth would not be removed from the ion-exchange column used to separate Lilly's A16886I and A16886II factors from the broth unless a sufficient volume of eluant, which is not disclosed by Lilly, is used (brief, pages 12-17). Appellants further argue, in reliance upon the Hermann declaration (exhibit 14), that any clavulanic acid removed from the column would be destroyed in the next steps of Lilly's isolation process (brief, page 17). These arguments are not persuasive because they are directed toward the fate of the clavulanic acid after the fermentation step. In so far as the § 103 rejection of exemplary claim 42 is concerned, the relevant issue is whether clavulanic acid necessarily is formed during the fermentation step along with Lilly's desired products. As pointed out in the prior board decision (exhibit 10, page 8), appellants' claim to clavulanic acid does not

include any purity limitations and thus does not exclude clavulanic acid present in a fermentation broth.

Appellants argue that Lilly discourages use of fermentation times greater than 72 hours by noting that the maximum production of antibiotic occurs within 36-72 hours (brief, page 18). Appellants point out that fermentation times of 3 to 5 days are desirable for the production of clavulanic acid (*see id.*). Appellants also argue that the declaration by Holmes (exhibit 15) indicates that small changes in fermentation conditions have a profound effect on the products formed (brief, page 19). These arguments are not convincing because the relevant question is not whether Lilly carried out the fermentation for the time which is most desirable for making clavulanic acid but, rather, whether, when fermentation is carried out for 66 hours as in Lilly's example 17 and the products desired by Lilly are produced, clavulanic acid necessarily is also produced.

Appellants argue, in reliance upon the Pfizer tetracycline cases,[7] that a trace amount of clavulanic acid in

[7] The Pfizer tetracycline cases relied upon by appellants are (brief, page 23): *United States v. Pfizer Inc.,* 498 F.Supp

Lilly's fermentation broth would not render unpatentable appellants' claim to clavulanic acid (brief, pages 20-22). This argument is not well taken because appellants' specification (page 19, lines 3-7) indicates that clavulanic acid is effective at a peak blood level as low as 0.1 Fg/ml, whereas in the Elson declaration (exhibit 16), when cephamycin C is produced, the level of clavulanic acid is 0.536 to 373.0 Fg/ml. Thus, the clavulanic acid produced in the experiments in the Elson declaration does not appear to be a non-recoverable, trace amount of no practical significance as in the Pfizer tetracycline cases. *See Chas. Pfizer & Co. v. Barry-Martin Pharmaceuticals, Inc.*, 241 F.Supp 191, 193, 145 USPQ 29, 31 (S.D. Fla. 1965).

For the above reasons, we find that appellants' claim 42 is *prima facie* anticipated by Lilly. Appellants argue that clavulanic acid produces unexpected results (brief, pages 25-

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28, 210 USPQ 673 (E.D. Pa. 1980), *aff'd*, 676 F.2d 51, 216 USPQ 1056 (3d Cir. 1982); *North Carolina v. Chas. Pfizer & Co.*, 384 F.Supp 265, 182 USPQ 657 (E.D.N.C. 1974), *aff'd*, 537 F.2d 67, 189 USPQ 262 (4th Cir.), *cert denied*, 429 U.S. 870 (1976); *Chas. Pfizer & Co. v. Barry-Martin Pharmaceuticals, Inc.*, 241 F.Supp. 191, 145 USPQ 29 (S.D. Fla. 1965).

26). This argument is not convincing because anticipation is the epitome of obviousness, s*ee In re Fracalossi*, 681 F.2d 792, 794, 215 USPQ 569, 571 (CCPA 1982) ("Though the PTO spoke in terms of obviousness, the lack of novelty from the claimed invention is a fact. Moreover, lack of novelty is the ultimate of obviousness. ... An old composition cannot be converted into an unobvious composition simply by inept references to obviousness."), and evidence of unexpected results is not relevant to anticipation. *See In re Malagari*, 499 F.2d 1297, 1302, 182 USPQ 549, 553 (CCPA 1974). Accordingly, we sustain the examiner's rejection of claims 36, 37 and 40-45 under 35 U.S.C. § 103.

Rejection of claims 38 and 39
under *35 U.S.C. § 103*

Claims 38 and 39 recite, respectively, clavulanic acid and potassium clavulanate, each being free of recited compounds which, appellants' specification states (page 3, lines 4-9), are antibiotics produced by *Streptomyces clavuligerus*, which is the microorganism which produces clavulanic acid (specification, page 1, lines 1-3).

The examiner argues that since clavulanic acid was

identified as an antibiotic, one of ordinary skill in the art would have been motivated to purify it because purification of prior art known compounds is well within the capabilities of the skilled artisan (answer, page 4). This argument is deficient in that the examiner has not established that it was known in the art that clavulanic acid and potassium clavulanate are antibiotics. The identification as an antibiotic referred to by the examiner appears to be that carried out by appellants. Hence, the record indicates that in making the rejection, the examiner relied upon impermissible hindsight based on appellants' specification. *See W.L. Gore & Associates v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983); *In re Rothermel*, 276 F.2d 393, 396, 125 USPQ 328, 331 (CCPA 1960). Accordingly, do not sustain the examiner's rejection of claims 38 and 39 under 35 U.S.C. § 103.

DECISION

The provisional rejections of claims 36, 37 and 41-45 under the judicially created doctrine of obviousness-type double patenting over claims 35 and 36 of copending

Application 08/417,628 and over claims 36-42 of copending Application 08/418,055, are affirmed. The rejection of claims 36, 37 and 40-45 under 35 U.S.C. § 103 over Lilly is affirmed. The rejection of claims 38 and 39 under 35 U.S.C. § 103 over Lilly is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

BRADLEY R. GARRIS)
Administrative Patent Judge)
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TERRY J. OWENS) BOARD OF PATENT

Administrative Patent Judge	)	APPEALS AND
	)	INTERFERENCES
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